

149



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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/890,416	07/27/2001	Yukio Yamori	SAEGU85.001A	1599
20995	7590	05/14/2004	EXAMINER	
KNOBBE MARTENS OLSON & BEAR LLP			ZUCKER, PAUL A	
2040 MAIN STREET			ART UNIT	
FOURTEENTH FLOOR			PAPER NUMBER	
IRVINE, CA 92614			1621	

DATE MAILED: 05/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/890,416	Applicant(s) YAMORI ET AL.	
	Examiner Paul A. Zucker	Art Unit 1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 January 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-3,7-11 and 19-29 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-3,7-11 and 19-29 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 20 January 2004 has been entered.

Current Status

2. This action is responsive to Applicants' amendment of 20 January 2004.
3. Receipt and entry of Applicants' amendment is acknowledged.
4. Applicant's cancellation of claims 4-6 and 12-18 is acknowledged.
5. Claims 1-3, 7-11 and 19-29 are pending.
6. The rejection under 35 USC § 102 (b) set forth in paragraph 10 of the previous Office Action in Paper No 8 is withdrawn in response to Applicants' amendment.

New Rejections

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

7. Claims 19, 26, 27 and 29 are rejected under 35 U.S.C. 102(b) as being anticipated by Ruf et al (Arteriosclerosis, Thrombosis and Vascular Biology, Platelet Rebound

Art Unit: 1621

Effect of Alcohol Withdrawal and Wine Drinking in Rats. Relation to Tannins and Lipid Peroxidation, 1995, 156(1), pages 140-144). **NOTE:** For the purposes of this rejection the dictionary definition of "cerebral apoplexy" as "stroke" is employed.

Ruf discloses (Page 140, column 2, lines 7-12 (not including abstract)) that the alcohol-withdrawal rebound effect in alcoholic subjects results in an increased risk of stroke. Ruf discloses (Page 142, column 2, lines 8-19 (not including table) and column 1, bottom, Fig. 2) that wine and grape seed extract exert a protective effect against platelet aggregation (the putative cause of the rebound effect). Ruf further discloses (Page 140, column 1, lines 18-20 (not including abstract)) that wine tannins contain resveratrol (a compound of formula 1). The ethanolic solutions of tannins from grape seed extract disclosed constitute a pharmaceutical composition. Wine, of course, is a food product derived from plants of the Vitaceae family. Claims 19, 26, 27 and 29 are therefore anticipated by Ruf.

Examiner's Response to Applicants' Remarks with Regard to This Rejection

8. Applicants argue (Amendment, paragraph bridging pages 6 and 7) that the amount of tannins contained in the grape seed extract added to the wine administered to rats by Ruf must be less than the instantly claimed amounts since rats could not consume enough wine daily to achieve the instantly claimed dosages. The Examiner disagrees with Applicants' argument because Applicants' calculations ignore the significant amounts of tannins (including resveratrol) contained in the wine itself.

Art Unit: 1621

Applicant's arguments filed 20 January 2004 have been fully considered but they are not persuasive for the reasons presented above.

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

9. Claims 1-3 and 7- 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hirschberg (WO 99/35917-A1 07-1999).

Instantly claimed is a composition comprising a pharmaceutically acceptable carrier and a stilbene of formula (1), in an amount 0.1 to 5% by weight, wherein the composition is in the form of a food product, in particular a juice.

Hirschberg teaches (Page 1, lines 18-23) methods for infusing compositions including phytochemicals and nutraceuticals (food/pharmaceutical compositions) into food products including juices. Hirschberg teaches (*ibid*) that the resulting food products can be used to alleviate dietary insufficiency or in the prevention or treatment of disease. Hirschberg further suggests (Page 3, lines 19-24) the use of resveratrol (a stilbene of instant formula (1)) along with vitamins in the infusion solutions. Hirschberg specifically teaches (Page 10, line 22 – page 11, line 2) the use of vitamins A, B, C, D, E and K in the infusion solutions as well.

The differences between the compositions taught by Hirschberg and the compositions instantly claimed are that:

- a. Hirschberg does not exemplify the use of resveratrol in juice compositions;
- b. Hirschberg does not set forth specific amounts of the active components.

Hirschberg, however, provides a clear suggestion to use resveratrol in the juice compositions that he teaches. One of ordinary skill in the art would have been motivated by this suggestion to make the instant invention. Hirschberg is silent with regard to the amount of resveratrol to employ. Thus one of ordinary skill in the art would have been compelled to perform routine experimentation in order to determine the instantly claimed optimum amounts of resveratrol to employ. Such experimentation is well within the capabilities of one of ordinary skill in the art. Therefore, in the absence of unexpected results, the amount of resveratrol employed cannot confer patentability.

There would have been a reasonable expectation of success since Hirschberg teaches the suitability of resveratrol for this purpose. The instantly claimed compositions would therefore have been obvious to one of ordinary skill in the art.

Examiner's Response to Applicants' Remarks with Regard to This Rejection

10. Applicants argue (Amendment, page 7, 2nd-5th full paragraphs) that Hirschberg does not teach the instantly claimed amount of the amount of resveratrol. The Examiner agrees but points out Hirschberg's silence, in fact, would have required

Art Unit: 1621

experimentation in order to determine the optimum amount of resveratrol to employ, as pointed out in the rejection above.

Applicant's arguments filed 20 January 2004 have been fully considered but they are not persuasive for the reasons presented above.

11. Claims 1-3, 7-11, and 20-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Mizutani et al (Biochemical and Biophysical research Communications 1998, 253, pages 859-863) and further in view of Caspar et al (WO 00/38620-A2 07-2000) and further in view of CN1127070 (07-1996, provided by Applicants).

Instantly claimed are food and pharmaceutical compositions comprising stilbene derivatives and methods for their use in treating and preventing the loss of bone due to osteoporosis and periodontal disease.

Mizutani teaches (Page 859, left column, first two sentences after abstract) that osteoporosis associated with estrogen deficiency after menopause is the most common cause of age related bone loss. Mizutani further teaches (Page 860, FIG.2, bottom right) the effect on ALP (Alkaline Phosphotase) activity of treatment of osteoblastic (bone forming) MC3T3-E1 cells with resveratrol (3, 4', 5-trihydroxystilbene, corresponding to instant formula (I)). Mizutani further teaches (Page 859, bottom right, last sentence) pharmaceutical compositions comprising

Art Unit: 1621

0.1% BSA, vehicle and/or varying amounts of resveratrol. Mizutani further specifically teaches (Page 862, left column, last sentence) using resveratrol for the treatment of osteoporosis. Mizutani teaches (Page 859, right column, lines 10-13) that resveratrol (3, 4', 5-trihydroxystilbene, corresponding to instant formula (I)) is derived from grape cultivars (plants of the vitaceae family)

The difference between Mizutani and the instant invention is that Mizutani's teaching is limited to treatment of bone loss due to menopause while treatment of periodontal disease (alveolar bone loss) and use of resveratrol in foods is also instantly claimed.

Caspar, however, teaches (Page 2, line 12 – page 3, line 3) the use of resveratrol for the treatment of periodontal disease. Caspar further teaches (Page 5, line 3-page 8, line 9) pharmaceutical compositions comprising resveratrol. Caspar teaches (Page 5, line 15-19) rinses (mouthwash), sprays, pastes and gels as dosage forms as well.

The difference between the combined teachings of Mizutani and Caspar and the instant invention is that neither Mizutani or Caspar teach the use of resveratrol in foods is also instantly claimed. Caspar is silent with respect to employing resveratrol in food compositions.

CN1127070, however, teaches (Abstract, lines 5 and 7-10) a composition in the form of food product (milk powder) comprising resveratrol (3, 4',5-trihydroxystilbene,

Art Unit: 1621

corresponding to instant formula (I)). CN1127070 further teaches (Abstract, lines 7-10) is use in the treatment and prevention of coronary disease and osteoporosis.

The motivation would have been to incorporate the bone loss treatment disclosed by Mizutani along with the teachings of CN1127070 to turn compositions for the treatment of menopausal and alveolar bone loss into food products that would present a more attractive form of administration of the compositions and would lead to better patient compliance. There would have been a reasonable expectation for success would all limitations of the invention are taught by the references and all are directed to use of resveratrol.

Thus the instantly claimed compositions would have been obvious to one of ordinary skill in the art.

Examiner's Response to Applicants' Remarks with regard to this Rejection

12. Applicants have presented arguments with regard to this rejection. The Examiner responds below:

- a. Applicants argue (Amendment, page 8) that an "obvious to try" standard has been employed by the Examiner in the subject rejection. The Examiner disagrees. All of the cited references specifically teach the use of resveratrol for the treatment of bone loss.
- b. Applicants further argue (Amendment, paragraph bridging pages 8 and 9) that Mizutani, Caspar and CN1127070 would not lead one of ordinary skill in the art to expect increases in bone breaking load and strength. The Examiner

Art Unit: 1621

agrees with Applicants but points out that these features are not limitations of the instant claims. The combined references would, however, lead one of ordinary skill in the art to employ resveratrol to treat osteoporosis and alveolar bone loss as is instantly claimed.

Applicant's arguments filed 20 January 2004 have been fully considered but they are not persuasive for the reasons presented above.

Conclusion

13. Claims 1-3, 7-11 and 19-29 are pending. Claims 1-3, 7-11 and 19-29 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Paul A. Zucker whose telephone number is 571-272-0650. The examiner can normally be reached on Monday-Friday 7:00-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann R. Richter can be reached on 571-272-0646. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Art Unit: 1621

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

A handwritten signature in black ink, appearing to read 'Paul A. Zucker', is written over a horizontal line.

Paul A. Zucker, Ph. D.
Patent Examiner
Technology Center 1600